



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,197	12/09/2005	Richard Joseph Fagan	C & R-104	1804
23557 7590 11/07/2007 SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950			EXAMINER MOORE, WILLIAM W	
			ART UNIT 1656	PAPER NUMBER
			MAIL DATE 11/07/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/538,197

Applicant(s)

FAGAN ET AL.

Examiner

William W. Moore

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-69 is/are pending in the application.
- 4a) Of the above claim(s) 49-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48 and 67-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>20061002</u> | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1656

described by the claims known to the inventors at the time the application was filed. It is agreed that the polypeptide having the amino acid sequence set forth in SEQ ID NO:22 comprises two catalytic domains each of which shares a significant degree of amino acid sequence homology with members of the trypsin family of serine proteases, yet claims 48 and 67-69 lack utility because there is no disclosure in the specification of any specific and substantial *in vitro* utility for an isolated polypeptide having the amino acid sequence set forth in SEQ ID NO:22, and the specification discloses no specific and substantial *in vivo* utility for an isolated polypeptide having the amino acid sequence set forth in SEQ ID NO:22.

Specifically, the specification cannot identify any particular substrate that is recognized and cleaved by either of the proposed serine protease domains within SEQ ID NO:2, whether *in vivo* or *in vitro*, nor can it identify a specific cellular, extracellular, or physiological function provided by either of the proposed serine protease domains. While the specification proposes at page 8, lines 8-12, that "screening methods" may be designed to identify compounds that are effective in the treatment and diagnosis of disease" once some function of the polypeptide having the amino acid sequence of SEQ ID NO:22 has been identified, and further propose a litany of diseases in the paragraph spanning pages 8 and 9 with which the polypeptide having the amino acid sequence of SEQ ID NO:22 might eventually be found to be associated, such suggestions of diagnostic and prognostic uses for the claimed polypeptide are not specific because there is no disclosure of any specific disease state or medical condition that actually can be diagnosed. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific *in vivo* utility that is substantial. Indeed, the specification's diffuse assertions indicate the contrary; that Applicant knew no specific utility for either native polypeptide encoded by claimed nucleic acid sequences at the time the application was filed that would permit an immediate use by the public of a disclosed nucleic acid sequence, or any use by the public of an expression vector or cell comprising a disclosed nucleic acid sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1656

Claims 48 and 67-69 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 48 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the preparation of the peptides and polypeptides having the particular amino acid sequences set forth in SEQ IDs NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, and 26, does not reasonably provide enablement for the preparation of generic proteases having amino acid sequences that diverge at as many as 114, or even 57, unspecified positions from the amino acid sequence set forth in SEQ ID NO:22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

At least clauses 7-10 of claim 48 contemplate arbitrary assignments of any or all of amino acid substitutions, additions or deletions in a claimed, generic, protease at as many as 20%, or 10% of the 567 amino acid positions throughout SEQ ID NO:22. This rejection is stated under the first paragraph of the statute because the specification cannot support introduction of such numerous alterations in the amino acid sequence of SEQ ID NO:22, where amino acid insertions, deletions, or substitutions may occur anywhere, in any combination or in any pattern, within SEQ ID NO:22. Mere sequence perturbation cannot enable the design and preparation of a myriad of divergent polypeptides that might be proteases where the specification fails to teach even the nature of the proteolytic activity that is to be retained, e.g., by identifying a substrate. Neither the specification nor the prior art made of record herewith provide adequate guidance for selecting 114, or even 57, amino acid sequence within SEQ ID NO:22 that might be altered, nor the nature of the alterations, that would permit proper folding of either or both of the catalytic domains indicated by the specification that would allow them to retain their undisclosed function(s).

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a **reasonable correlation** must exist **between the scope asserted** in the claimed subject matter and **the scope of guidance the specification provides**. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with

Art Unit: 1656

the degree of unpredictability of factors involved in physiological activity of small peptide hormone). **The Federal Circuit has approved this standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).** Applying several of the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

- a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of SEQ ID NO:22 to the extent indicated in clauses 7-10 of claim 48,
- b) the specification lacks working examples wherein the amino acid sequence of SEQ ID NO:22 is altered to the extent indicated in clauses 7-10 of claim 48,
- c) in view of the prior art publications of record herein concerning very similar polypeptides, the state of the art and level of skill in the art do not support such alteration, and,
- d) unpredictability exists in the art where no members of the class of serine proteases the specification suggests is represented by SEQ ID NO:22 have had as many as 114, or 57, amino acids specifically identified for concurrent modification, as indicated in clauses 7-10 of claim 48.

Thus the scope of subject matter embraced by the phrases, "at least 80%/90% identity with", is unsupported by the present specification even if taken in combination with teachings available in the prior art.

Claims 48 and 67-69 are additionally rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

While the specification discloses particular functional fragments of the polypeptide having the amino acid sequence set forth in SEQ ID NO:22, e.g., SEQ ID NO:26, the specification fails to exemplify or describe the discovery or preparation of the genus of fragmentary or "functionally equivalent" polypeptides that diverge from the polypeptide having the amino acid sequence set forth in SEQ ID NO:22 at as many as 20%, or even 10%, of the 567 amino acid positions therein at any conceivable set of 114, or 57, amino acid positions dispersed in any pattern throughout SEQ ID NO:22, according to clauses 7-10 of claim 48. Indeed, the specification discloses no particular function that must be retained by such randomly altered fragments or equivalents. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The "test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the Inventor had possession at that time of the . . . claimed subject matter", *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983), and, in 2001, the USPTO issued Guidelines governing its analysis of compliance with the written description requirement. In these

Art Unit: 1656

Guidelines, the USPTO states that an applicant may comply with the written description requirement by "show[ing] that an Invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . , i.e., complete or partial structure, other physical and/or chemical properties, function characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." **Guidelines**, 66 Fed. Reg. 1099 at 1106 (5 January 2001). The Federal Circuit adopted the USPTO's standard for determining compliance with the written description requirement In *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). The specification does not disclose the design of the broad genus of polypeptides embraced by, at least, clauses 7-10 of claim 48, which state no particular functional or structural requirements, nor does the specification otherwise disclose the source of generic polypeptides meeting the limitations of these clauses.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48 and 67-69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations of "functional equivalent" in claim 48 render the claim, and claims 67-69 depending therefrom, indefinite because they provide no structural basis for a determination of the extent of structural equivalency of a polypeptide to the polypeptide of SEQ ID NO:22 and the term "functional equivalency" is meaningless where the specification discloses no particular function for the polypeptide of SEQ ID NO:22. Thus the artisan and the public seeking to ascertain the metes and bounds of intended subject matter have no starting point with which to determine the structure or the nature of the polypeptide intended by the claims. Deletion of all references to "functional equivalency" will overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 48 and 67 are rejected under 35 U.S.C. § 102(e) as being anticipated by Goddard et al., US 6,916,648, made of record herewith.

Art Unit: 1656

Goddard et al. is the US equivalent publication to WO 00/53756, cited in Applicant's IDS filed 2 October 2006, and is available as prior art in view of, at least, the 24 October 2001 filing date of the US utility application on which the patent issued. Goddard et al. disclose, in their SEQ ID NO:132, the amino acid sequence of a human serine protease that shares 89.3% identity with SEQ ID NO:22 from position 39 through position 548, and comprising amino acid sequences identical to those of SEQ IDs NOs:8, 10, 12, 14, 16, and 18 herein, meeting limitations of claims 48 and 67.

Claims 48 and 67 are rejected under 35 U.S.C. § 102(e) as being anticipated by Plowman et al., US 2002/0064856, made of record herewith.

Plowman et al. is the US equivalent publication to WO 02/00860, cited in Applicant's IDS filed 2 October 2006, and is available as prior art in view of the 26 June 2000 filing date of their priority US provisional application. Plowman et al. disclose, in their SEQ ID NO:86, the amino acid sequence of a human serine protease that shares 93.2% identity with SEQ ID NO:22 from position 17 through position 548, and comprising amino acid sequences identical to those of SEQ IDs NOs:4, 6, 8, 10, 12, 14, 16, 18, and 24 herein, meeting limitations of claims 48 and 67.

Claims 48, 67, and 68 are rejected under 35 U.S.C. § 102(e) as being anticipated by Madison et al., US 2003/0134298, made of record herewith.

Available as prior art in view of the 5 July 2001 filing date of their priority US provisional application, Madison et al. disclose, in their SEQ ID NO: 16, the amino acid sequence of a human transmembrane serine protease having significant sequence identity with human matriptase, which amino acid sequence shares 96.7% identity with SEQ ID NO:22 from position 17 through position 567 and comprising amino acid sequences entirely identical both to SEQ ID NO:26 herein as well as SEQ IDs NOs:4, 6, 8, 10, 12, 14, 16, 18, 20 and 24 herein, meeting the limitations of claims 48, 67, and 68. It is noted that amending claims 48, 67, and 68 to require that a polypeptide comprise, or consist of, the amino acid sequence of SEQ ID NO:22 will overcome this and other prior art rejections, as well as rejections of claims herein under 35 U.S.C. § 112, first paragraph, for lack of adequate written description and for lack of enablement as to making, leaving only the issues of a lack of patentable utility under 35 U.S.C. § 101 and lack of enablement as to use under 35 U.S.C. § 112, first paragraph, to be resolved.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Art Unit: 1656

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashed/
Nashaat T. Nashed, Ph.D.
Primary Examiner, Art Unit 1656


William W. Moore
2 November 2007

-continued

<222> LOCATION: (1)...(1954)

<223> OTHER INFORMATION: N refers to any nucleotide.

<400> SEQUENCE: 33

```

gangattcct nccnctnccc attgaaaaga ggatggattn gancatatgg gtgtgcctgc      60
aagaagataa gtcaatataa tgtaactcag aaaaatcaat tcccaaatg aatacccnc      120
aatcwataca aaaaawattg awagattttt kggtkgacat tactaacttt ttgaggcna      180
agacatcmat ccmrgcmgga tgcctggtga ctatggtgkt gattccatta ttaggtatga      240
gatttyttaa tcgaattaac cyccaccttt aawatagaag ctgatgcttt attactaaca      300
gaaggacga ttmaccagta tatctcataa arkwcmttct tttattgttg ataaaaaaa      360
ttaccaatg ttaccaaatt ttggattaga aatgattctt aataaagaaa ataaaggctg      420
ggtaaagcct tcttttattg aatttattaa atttgaaatc aatcctgaat atatagaag      480
cagtacaaaa aataaagatt acgcgattct tgaaaatcta ataaataatg gagtggagt      540
ttggagagaa aataatcatc tatgttttga gtttttttat gaaactcata caaatgaanc      600
aataaaaaaa atagtgtttt caccgaaat actttttaac tctctagata aaggtaaacg      660
atactttcca agtagctgcc agcaaaaaaa cagtctatat caaacggaag ttgagaagtt      720
tccatataat cttattcaag gatttagagt ggaaatgcca gtcaatattg aaattttaaa      780
taaagcattt aatcatttgg ttaacacata ttcaatttcc agaacaaaag caatgttgat      840
caataagcaa tggattcagg taatacatga tggtttatca gtaagatgcy aaganaatta      900
yatacgaagg attatctgca ggaaaaagat ttacgcaac aactaatnag tatttcaaaa      960
agagcaaggt aaaaaattat ttgatatcga taatctgcct ttattaaaaa tttattttat      1020
ccataatggt aagacttag cagctatttt tgttcacgcy catcattttt gtgccgatgy      1080
atttacattt tttcttttcc agaaagaatt tcatgatact trtgaaagta ttatraacgy      1140
antggrwat ccggaacgk gttcsawaaa gtgatggctg aatatggcca ctttgcattg      1200
tgtgaatata atcccaaaaa caaggagctg acaaaaaaact ggcttgataa aattcgagat      1260
aaaaattttt ctttaaaatt taaagataag aaagactatg tcggtcact gtcaagtga      1320
gaaaaaatta ttgagctaga agtttctgta aatatgctgy aaaaattaag attatttaat      1380
gatgcgaata ataccacact gacgcaattg ctatgttgty ctgttgcaat tttactgtat      1440
cgctctcga ggctaccagt acccttgcaa atggteaaca gccgtagaga taaaatagaa      1500
tttgaataaa tgatgggtga ttttgcata actctgcct atggatttta ggaaccttc      1560
caaaagcatt ttctctattc cnggatggtg ccttttttaa gttattggaa aaanggaana      1620
aggcnttnaa tntcccccc naggattttt taaanggggt ttgatnntt tntcngggaa      1680
ccctcaanaa aaaaaaaatt tntttccaaa aaaaaaaggg gccctttaa ntccccatta      1740
agggaatttt ttaattttt taatttccg gnaaaaatta tttntttaaa ttccggaatt      1800
aaggccnaan tggaattaat tggnaaaatt tccantttgg gtttttaaaa aggggaaaa      1860
nccannaat ttgggtttcc ttaaaaaana aaaaagggg gngggcccc cggtgggttc      1920
ntnntgggg gnaaaaattt aaaaatttaa tttt                                     1954

```

<210> SEQ ID NO 34

<211> LENGTH: 2672

<212> TYPE: DNA

<213> ORGANISM: Endobugula sertula

-continued

```

ggctanacgc tctatccggt gggtaatatg aantaaaaca attcgtatatt tagaaataag 2820
gagcaggtac ctggtggtgc caacagagtt tgtattngaa tagnaccttc mccgctnctc 2880
gaatgggtat aagagtttta cntatactgg atatctnctg ccntcgttcc ttcgttatgg 2940
gagaaaagtn agatitttycc gataaatatn ccctggtnng caatataagg tggttagatat 3000
ntgaaagmca atttagantg cacaagggtt ttaccctgat agctttgata ttingtstatg 3060
catctaattg tntccacga tacgaaawta tatacagtat accctttccc aaagttagtc 3120
acatgctaac gcaaatggc nttgttaag ttgaatgaan ttactcngg atgaanggat 3180
ttgttactgt ttaccggtg tttgttagat ggcctttggt tatatgaaga ccctaccaat 3240
cgattggata atgtctgctt gttaaatggt gatcagtggt gatctatatt atttaaatca 3300
ggctttnaaa aatgttaaag actttgtttt accttttgaa aaacttaata ttgagcaaag 3360
tcaaagtatt attgtctctg agtggattaa tgaagacctg tctagtaatg nttgaaaatg 3420
tggtgaaaaa taatcanttg ttnnagaaat acaaatcac tcntgatncc gattactngt 3480
ggagnaataa aattagnnta caattnaaaa gacaantcmc wtggttanca caatagtatt 3540
ggaagaaaat atttttataa aattttagnn gggataaaaa gaaaattatn ggatttttct 3600
ccntaaacgc ccctttgatt ggagtttatg ggttggattc atattcgaac ctacmttgga 3660
anttaagat cattactcgg kragcmtyt tcyataaaac trgaasmtac tttkktmtky 3720
mawkatkraa yrmkackkm ractmtytgw kwcmccsay atsattcmag wtrascytar 3780
watrtcgmt arakwcccta ttacggaaga gataatgact ggaggtacgt caagggtaar 3840
aacagggcaa tcgaatsaka atgaacctat tgcgattatt ggtatgtcyt gtttatttcc 3900
aggtgaggtt acgacagttg atgagttctg ggaattatta atacaagaaa gacatgccrt 3960
tcaaccctta cctaagggaac gttggcaatg gccakaaggt gttgatccat cgggagcaca 4020
acttggcatt gatcaggggt gatttctgga tggattgat acccttgatg ccsacttctt 4080
tcgtatatcg agaaaagaag cggagttwat ggaccctcas caaagaaaac tacctggaat 4140
taarttgga ggtcatasag catgccggat ataaacccat cgytktttc tggtaaaaga 4200
natygyytc tatgtgggtt gctttgtcac cggtaattta tatgggagtt atttaactaa 4260
aagtgacca angccctaaa aaccaaccgg naagccctat ttkcatgacc argtartana 4320
ttgttggtcg tytttcccc aataanaatt ttcctatttt ntattaattt tttaaargtg 4380
ccmcscstcc tctwtctgat wccngcctt ttcaaryagt tttaggttgc ctwtttgacc 4440
caancarttt tatgcgnatt caattcgggg nangngtga atcaggcttc tgggggntg 4500
gggaycaatt waatrtcccc tccsmrtgaw accggtttct tnattayywa gcaggtntgt 4560
tntcaaaatc ngggaatgta aaccttnga tccaccgcc gttggtttn tncctgggna 4620
aagggggcgc tnttcttttt ttnaatcntt ttctcanccc nattttaaaa ngattgtttt 4680
ttnggggttt taaagggggg agatnaaat ngggggcaan cattnnttac ggcctaacc 4740
tnng 4744

```

<210> SEQ ID NO 33

<211> LENGTH: 1954

<212> TYPE: DNA

<213> ORGANISM: Endobugula sertula

<220> FEATURE:

<221> NAME/KEY: misc_feature

-continued

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)...(2672)

<223> OTHER INFORMATION: N refers to any nucleotide.

<400> SEQUENCE: 34

```

anccgaaaaa naccnaaag gnggcccggc cntgtcctnc gagtgcatna taaaaaanc 60
agtnataagn nggnnacaat antcatgccc cgcgcccnc gnaagnaacc tnantgggtt 120
naaggcttca agggcatcgg tcaagggaacc ttctggcggg cttttgctgt gcgacaggct 180
cacgtntaaa aaggaaataa atcatgggtc ataaaattat cacgttgtcc gggcgcgggc 240
acgaatgttc tgtatgcgct gtttttccgt ggcgcgttgc tgtctggtga tctgccttct 300
aaatctggca cagccgaatt gcgcgagctt ggttttgctg aaaccagaca cacagcaact 360
gaataccaga aagaaatca ctttaccttt ctgacatcag aagggcagaa attgcccgtt 420
gaacacctgg tcaatacgcg ttttggtgag cagcaatatt gcgcttcgat gacgcttggc 480
gttgagattg atacctctgc tgcacaaaag gcaatcgacg agctgarcym scrmaktygk 540
gmcmccgkmw cctwmrarst twttcscaaw rragkkywt tmawmaagm cscygakrky 600
gswwtggwr ctawccacgm arcssmwty gaaamaccka rkcyggnktw csrawawmwa 660
cmrsmycasc cttggwawmm armrwsmtga syywgckcw g aamaakgtwa ccstcrkgk 720
cgmtwvghkc aawkttwmac cysrwrwrr ymcmaematt garrcattgm ycgraaccsc 780
gmtgaaaaan negctghntg nnaatgtrvg gcgtntggat gtchcaagc aaatggcasc 840
agacaangaa agcgatggat gaactnnngg ctctcttatg tccgcccgc caktcatgat 900
ggaatgttcc ccccggttgg tgttatctgg caccagtgcc gtcgatagnt antgcnaant 960
tngantaant tnattnatca tttngncggg ntcctttnc gmgcatcnc gccttgttta 1020
cggggcgggc acctcgnccg gttttcgcta tttatgaaa ttttcgggt taaggcggtt 1080
ccgttcttct tctcataac ttaatgtttt tattanaat accctctga aagaaggaa 1140
acgacagggt ctgaaagcga gctttttggt ctctgtctgt tctttctct gttttgtcc 1200
cgtggaatga acaatggaag tcaacaaaa gcagagctta tcatgataa gcggtcaaac 1260
atgagaatcc gcggccgcat aatcagactc actatagga tcatatttat ggtgttatta 1320
aaggaggtgc catcaatcat ggtggcaaaa ccaatggcta tagtgtcct aatccggata 1380
agcaacagcg tgcattagt gaggctttgc agcgggtca aatagctct catcaagtca 1440
gttatgtaga agcgcattgt gcgggaagcc gtttagcga ccaatagaa attacggctc 1500
tcagcaaacg atttaacaat gttagtgcgc aatttaantgt gaaaagtga gccaatcaat 1560
cgtgttttat tggctcggta aaatccaata taggaactg tgaatctga gcagggaent 1620
gccagtatta gcaaatgatt gctacaaatg aaacatgggc aaatagtcgc gtccttgcat 1680
tcaaaagaac tgaatcccaa tattgatttt tcagcaactc cctttgtggt taaccaagaa 1740
ctgcgcgatt ggcagagacc gctgattgat ggaanaacag tgccgagagt tgcgggtgtc 1800
ttttcatttg gggcaggttg ttccaatngc nttacgtggt gattgaagag tatattgcga 1860
agataccgac aaataacacc agggaaatcta taaaccatag gtctattatt ccattatcag 1920
cacgaactgc tgagcagttg cggaatattg ccagtagatt gctggcattt attgaaaaga 1980
acaagcaaga cagcgtggtt acccccttaa tagatattgc ttatacattg caggtaggac 2040
gcgaagcaat ggatgaacgc ttgggggtta ttgtgagttc aaccgatga attagtcgaa 2100

```

-continued

gaactacgaa gatattctca aacacacgat gatatggaag agctttatcg aggtcaggtt 2160
aatcgatatg aagacacctt tcttactatg gcggctggat ggaagatctc tcttgaggtt 2220
atccccacca ttggggatta aaaaacgaaa aactggctctt aagtttaatg ccaattattt 2280
gggattttaa aggggtcttt gtggatttaa wttkgggrkr agwtatassw tkkytmcca 2340
aargrkgtw ktcycagcr matkarmkka ytacctrtec ytyygcrgs matattttta 2400
rgwtktamm swtyrnmccc tctwccctyt tktgtrccc aggnccaaa tttattttng 2460
tttnggggga atttngtttt aaaaaagaat tcggttaanc ccacctnccn ttaaaacttc 2520
attttggggg gnaatgggtt ttattgnaa cccattccna aaacaaaaa ngggcctttt 2580
tttttccat tccnaaaaaa accaaatttt gggccctttt ttgggggggg gaaaaaaa 2640
accnaangg gaaaaaattt ttttaaaa aa 2672

<210> SEQ ID NO 35
<211> LENGTH: 2132
<212> TYPE: DNA
<213> ORGANISM: Endobugula sertula
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(2132)
<223> OTHER INFORMATION: N refers to any nucleotide.

<400> SEQUENCE: 35

nnnnanttc cnattccctt gggcggaat ttttgccca ggnccgnat aaccaagga 60
ccctttttn gggcccttaa aaaaacccaa ttttccctt ttaatcccc cgaataaag 120
aacctttccc aaaaaaggg naantgaan tgggggnan cntgggaaat cccaagccaa 180
aaaaaggccc aaymtcgccc waraacrkkc cawaatsss gavaasmcyy ccagawarwa 240
ttkwtkrwa mrawcyagy wmscamatc rgrtgttwta tgyrrssrg wmyawwtraa 300
aarymtcca wytkttkss grtcaatka tgsrkwtty tcaaymttg gactcmcyym 360
tcmmmwttt gaaaacmyw attatakktr taagggggc aaataatcaa tgttgatat 420
ggttaamccg ataaaaaaa gcctcaataa atttttctgc caacaactaa gacagctcta 480
caataaacat aaagcaata atgagtcctt gtgattattt cccatgaaaa aaacaatggc 540
attttaatag atagatctca tactgaatcg aatattgcca ttataggtat atcaggggtg 600
tttccgatg caaaaaatgt taatgaattt tgggaaaatt taaaaaatgc tgcataagt 660
gttaaagaaa ttcctataa ccggtcttg gatattgata attactttga tacttcttcg 720
caaacacatg cacaggaata tgttaacaa ggagcatttt tagaaaatat cgatcttttt 780
gatccgctgt ttttaatat ttctccggtg gaagcagagc ttatggatcc aactgaacga 840
ttttccctc aggaatcctg gaaagcgatt ganangatgc tggttatgat gcacaaact 900
ntaagtggaa aacgntntgg ggggtatttg cctgtgcaa gggagactac catgccatta 960
ttcacaagca ggataaaact cgtatcatga ccaactgactc tatgcctct gccaggttg 1020
cttatttatt gaatttgnnt tagggcctgc agttcacgtt gatanccggc ttgttcacn 1080
gtctttggca gcaattgett acgcatgtga tagcctcatt cttagaaatt gtgatgttg 1140
cattgcagga ggtggaata tcaactcaac tcccagcctt ttgatcagtt caagtcaact 1200
tggtttgtg tcaaaagatg gccgatgta tgccttadat caacgtgcaa acygaacggt 1260
attaggggag gcggtascac cgattatttt aaaccctta caacaagcga ttgacgatgg 1320

-continued

tttgaccaat gagcttggtt taagcgctgt gscacaaacma tygkgtttga tcggstcark	2040
gaagtcacaaa tatagggcat tgtgagycas caagccggtg ttgcagctat tagcaaaagta	2100
ttgttacaaa tgcaacacgg gtcaaatagt cccttcttta cattcaaaag cattgaatcc	2160
caatattgat ttactgtga ctccctttgt agtaaaccaa gggttattgg actggaaacg	2220
acttgaagtt gaaggaaaga gggtrccgag aatkgctkky mwwckkyyt ttggggccgg	2280
tggtcacaat gcccatgtag tgattgagga gtacgttgcc agcaatgana agcaagagga	2340
ttttcaagga aaagtaatta tccctttatc ggcwatagac tskgatcar ctacaaraaa	2400
warkggatcg tttgcttaag tttatcraaa aaaatgaagc aaaraggtag ggaawtkagc	2460
ttaattgwtg ttgccgwawa cattgcaact tgggcgcgag gtcaatgara ggaacgtctg	2520
gnmcttngan ttgtaggaat cnaataccaa atgcttaang gaaagatttt agcaaaaggnt	2580
ttaaatactc agaaaatnga tgcacanaatt ttccggatag ttatcaaaag rcattttatc	2640
ggggttcgta ctgagacctg gtgcgttgra ttccgctatt ttttctgaag atgaagaata	2700
tgcccaacac gcttgatatt ttggattcaa aaaggtaaat actttaagnc tggcggagct	2760
ttgggtaaaa ggtgtgacta ttgattggaa taaatggtat aacgcattat taaccagaa	2820
taaatatttg aaaccntcgt cgtattagtt tgcnaacng tatccttttt ccagggatcg	2880
ttattggatt nccnaagtgc ttttccacaa ncaaacattt tctacagtaa ttgaggcaga	2940
cgccaacma aacattgaat gagctactgt gttttgaaga aaaatggcag gtgcaatcgg	3000
aactacatga ctctgttgca gatcaatcta atgttatcaa tacattaant tgttttttaa	3060
ctgagaaaga gcatcaaaaa gcattacaac aatcaatata attccatagc ccgaaaacac	3120
gattgatttt tatcagccag gctcaggctt atgagcagta ttcacatagc cactatgcgg	3180
ttaatccaga aataggaaag acgtaccaac aggcctttca acacattgtg aaaagtattc	3240
ataaaagtga tgtcacggac ataattgatt tatgggctct agaggatgaa cgctggatta	3300
cgtctcctct acctattgta tatcttttaa aaagtattga ggtttcttta ttaaaaccar	3360
aaaaattact atttgttga gaatttaaga caagcttakc rrcgagtgy acyykraakc	3420
cwrkgkkggw ttygmamrwy ckkwakagtt dgtgcaacsg ratwtkragg ttgcggtgtt	3480
attaraggcm rtggaaggta ctynaatccca tmcagtaca aagcaaatgg atctttggat	3540
agaaaaattg tggctgtcct taaaagccca aaaagtccat agtagcttat accaaaatgg	3600
tcgtagatat ttttctgaaa accccamccg ctgcaanctt gtcatgaacc aaagtattca	3660
aatgcttaca gggactttta ttgataacag stgcytgtgr aggactgggt tttgtcttyg	3720
cagattattt ttccaagaca tataaaatta atctgatatt ggttggcgc tctgatcttg	3780
ataaagagaa agswtcgsr ratwcrgrmt ykghwmaat caggtagtcg agtggtttat	3840
gttcagacgg atatctgcga tgaaaagaat ctccaattgg aattggatat tgcccaaaaa	3900
tattgtggcc ctattcaggg tgcattcat gccgcgggca tcattgatca gaagacaatt	3960
tttgaaaaaa gtcctgaaaa ctttcaagca gtattagccc ntaaaattca gggtagattg	4020
attctggata acgtattgtc agcgcaatca ctggatttta tatgttactt ttcttcaagc	4080
tcggctctat taggtgatgc aggatcatgt gattatgcaa tggctaactg atttttgatg	4140
gcccatgcac agtatagaaa tacctyggta tctgaargaa aamscaaggg raagacmctg	4200
ktwttcatt ggcccgcctg gaatgtgaaa ggaatgggat tgaatggact ggaatgagaa	4260

-continued

cgtgaaamca ragttctwty ttaagtcāaa gcgggcaasg tctattggac ataaaggaag 4320
 gttgtgaggt tattgaacac atttctggct caggattatt ytcagtgtcy tawattggst 4380
 ggkaggaāaa accngtatcw aacaattttt tgggtctcac acaagatgt ttctnacctc 4440
 acaagtgagt caagggcagg magtrawgaa cwwasrrewk kmykkrras keyamyaac 4500
 gagctgagat agaagacttt aagtgttgaa gaatgtatta ttttgactt aaaaactctg 4560
 attacagagc aacttaāaat acccatcagc tcatctggat gtagagagta atttagcaga 4620
 ttttggtttt gattcgggtca gtttagcaaa cttttcccggt gtttaagta ttcmctatca 4680
 ttycaawawt acgccrtstk tatttttcgg atatcctacc atagagcgty taarccgtta 4740
 ttttttaāaa gaacmcmctg cgsttatgga ggcgttttat cagcagāaaa aaacatywa 4800
 tagtaacaat acvctgtccg ntatagtcgy tcatgtcaaa gaaaagccgw caactgatct 4860
 aatatcatcc arcngcctct nccitttatt gcagatccat tgccccctca ggstattgag 4920
 agtattgatg agcctattgc cattattggt atgagtggtc gttttccaga agcgcgtacg 4980
 gnttaagca atgtgggaga ttttatccga aggtāaaagt sytgtgcagg agattcctat 5040
 agagcgcttt anattggcat gaattattat aacacccatc ggatgatgtt ygaanaandb 5100
 taatagtaaa tggagygcct gcattcctgg tattaagaa ttcatccac aatttttcga 5160
 aatttctcca agagaggcaa āaaarctgga cctcttcaa cggcwettat cacaggaatc 5220
 mtsgaatgca ttggwaaats ctgcttatgk wwwmywacrc wkvgmtmw tw aracratggg 5280
 ataytkkkt tggtrttgaw smaggktwtt atmmrrrymw gmtcaatkmar gwygacagca 5340
 cacwttwawc catmakrmta ttttrgcata cmgtytgsc agtwtytwtt arakyttaat 5400
 ggacmrrasa tggcwrtwaa wrccgwtgy tcttccgyw tggyygcrrt tcaccamgct 5460
 kacsysagtt tackwcarca agcaatkyga wrccgckawk gwccggcag cwwwyttrmw 5520
 mwyacrsk sawswkaws tggscwtgay ssawsgrgy mtgakmyac mwgawgsyat 5580
 amygawakac ckarnrtcam csygccāaks gcryagtomy tggakagsmw gytgwtgcar 5640
 tcgtaytgma acrwmtcttk agggktttcc āaaagggggt mmaaat 5686

<210> SEQ ID NO 32

<211> LENGTH: 4744

<212> TYPE: DNA

<213> ORGANISM: Endobugula sertula

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)...(4744)

<223> OTHER INFORMATION: N refers to any nucleotide.

<400> SEQUENCE: 32

gngatgagat tgatgagaat acttaatttg gtcgaanagg ccattacntc tatgattctt 60
 ggtgaattta taagccaatt aaccngtgat ttagtttggā atatgaāga acccgtttta 120
 tttgactatc ngaatattāa tactttatcg aatatgatcg agaatgaact cgaagctggt 180
 gaggtatagt tatgttagaa gttattaata gatactgcca tggatacgtā ttctgtccag 240
 tggatttggc cntagaagaa āaagggtttt ttgacctttt tacaaggaat agatacctta 300
 catttgāaaa aatāāāaca gaattāaatg ctaatagtgg ccatcttcaa gtagccttac 360
 gcatgttgca gtctgtttca tggatatcat gtgatgataa agggtatgta ctaacagatg 420
 cagcggacga aagāāāāā atatctagt attttataga gctttttaat ttctctatga 480

Art Unit: 1656

DETAILED ACTION

Priority

Applicant's claim in the Declaration of Inventorship and in the first page of the specification filed 9 June 2005 to priority under 35 U.S.C. § 119 of the 11 December 2002 filing date of the British patent application No. 0228957.7, and its successor International patent application PCT/GB03/005404 filed 11 December 2003, of which the current application is a National Stage filing under 35 U.S.C. § 371 is hereby acknowledged.

Information Disclosure Statement

Applicant's Information Disclosure Statement [IDS] filed 2 October 2006 is hereby acknowledged.

Preliminary Amendment

Applicant's Preliminary Amendment filed with the application on 9 June 2005 has been entered, canceling claims 1-47 and providing the new claims 48-69.

Election/Restrictions

Applicant's election without traverse of the invention of Group I, comprising claims 48 and 67-69 to the extent that they describe a protease having an amino acid sequence set forth in SEQ ID NO:22 and to compositions comprising same, in the reply filed 25 October 2007 is acknowledged. Claims 49-66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 25 October 2007.

Claim Objections

Claim 48 is objected to because of the following informalities: Several occurrences of the term "SEQ ID NO" are misstated in claim 48, e.g., at lines 5, 13, 21, 26, 46, 51-52. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 48 and 67-69 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

A claimed invention must possess a specific, substantial and credible *in vitro* or *in vivo* utility, but the instant application cannot identify any specific, substantial, utility for the invention